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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/628,158	07/28/2000	Raghnath Vitthal Chaudhari	5728	2931

7590 12/10/2004  
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EXAMINER

OH, TAYLOR V

ART UNIT PAPER NUMBER

1625

DATE MAILED: 12/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/628,158	<b>Applicant(s)</b> CHAUDHARI ET AL.	
	<b>Examiner</b> Taylor Victor Oh	<b>Art Unit</b> 1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 September 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2 and 8-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 8-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 July 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### ***Final Rejection***

#### **The Status of Claims**

Claims 1-2 and 8-21 are pending.

Claims 1-2 and 8-21 have been rejected.

Claims 3-7 have been canceled.

#### **Claim Objections**

The objection of Claim 21 has been withdrawn due to the modification made in the amendment.

Claim 20 is objected to because of the following informalities:

The phrase "dioxin/dioxin" is recited. The expression of "/dioxin" is redundant. The examiner recommends to remove "/dioxin". Therefore, Appropriate correction is required.

#### **Claim Rejections-35 USC 112**

1. Applicants' argument filed 9/27/04 have been fully considered but they are not persuasive.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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The rejection of Claims 1 and 21 under 35 U.S.C. 112, second paragraph, has been maintained due to applicants' failure to change in the amendment.

**Claim Rejections-35 USC 103**

Rejection of Claims 1-2 and 8-21 under 35 U.S.C. 103(a) as being unpatentable over Elango et al (U.S. 4,981,995) in view of Chaudhari et al (U.S. 6,093,847) .

The rejection of Claims 1-2 and 8-21 under 35 U.S.C. 103(a) as being obvious over Elango et al (U.S. 4,981,995) in view of Chaudhari et al (U.S. 6,093,847) is maintained for reasons of the record on 3/23/04.

***Response to Argument***

2. The applicants argue the following issue:

1. The Elango et al have used at least 10% of H<sub>2</sub>O based on the weight of IBPE, forming a bi-phasic system, thereby leading to a decrease of % selectivity (75% or below) and % conversion unlike the prior art 's selectivity is up to 99 % due to a homogeneous phase;
2. The prior art references do not use the pressure as low as 50 psig; further, the catalysts used by the applicants are very specific for a particular reaction so that one should not be assumed

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that it will work in another reaction or all catalyst will work in a particular reaction ;

3. The Elango et al has indicated that the presence /absence of dissociated hydrogen ion or halide ion in the reaction affects the % conversion and % selectivity of ibuprofen in the range of 33 to 99 % and 0 to 78 % respectively;

4. A change of acid from sulfuric acid to HBr affects the % selectivity of ibuprofen from 42-70 % to 59-85 % in examples of 11 to 17 of the Elango et al ;

5. Chaudhari et al discloses that the production reduces from 1190 /hr to 556/hr in the examples (8 and 9) as the reaction pressure decreases unlike the present invention the production rate is 1450/hr with up to 99 % conversion and up to 98.5 % selectivity at low pressure;

6. There is no motivation in the references to arrive at the current invention;

7. None of the prior art suggest that keeping the low pressure, low water content at a particular concentration or within a particular concentration ranges will lead to the results of the present invention.

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The applicants' argument have been noted, but these arguments are not persuasive. First, with regard to the first argument, the Examiner has noted applicants' argument. However, the secondary Chaudhari et al prior art has been used to supplement the primary Elango et al; furthermore, Chaudhari et al does indicate that, during the process of preparing ibuprofen, water (4% v/v) is present (see col. 4, example 3) in the reaction mixture containing ibuprofen, palladium catalyst with a phosphine ligand(see col. 1, lines 63-67), N-methylpyrrolidone (see col. 2, lines 61-65), thereby obtaining 98 % selectivity and 97.8 % conversion. Therefore, the combined prior art rejection is still relevant to the issues in the invention.

Second, with regard to the second argument, the Examiner has noted applicants' argument. However, on the contrary to applicants' assertion, the Chaudhari et al expressly indicates that the reaction process is conducted at pressures ranging between 50 and 1500 psig; both prior art have commonly used the palladium catalyst in their processes; therefore, applicants' argument regarding the specific reaction which requires the specific catalyst is irrelevant. Therefore, the prior art references are relevant to the claimed invention.

Third, with regard to the third and fourth arguments, the Examiner has noted applicants' argument. There is no doubt that there are many variables in the reaction process, which affect the % conversion and % selectivity of ibuprofen; however, applicants have not provided an unexpected result based

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on a side-by-side comparison data between the prior art and the current invention with the fixed variable. Until then, applicants' argument is persuasive. Also, there is nothing about the actual claimed limitations of the % conversion and % selectivity of ibuprofen in the claims. Therefore, the prior art references are still relevant to the claimed invention.

Fourth, concerning the fifth and seventh arguments, the Examiner has noted applicants' argument. However, from the specification of the current invention (ex. 8), the reaction is conducted at a pressure of 200 psig ; the GC data shows TOF of 222 /hr and 99 % conversion of 1-(4'-isobutylphenyl)ethyl chloride with an ibuprofen selectivity of 90 % ,whereas the Chaudhari et al reference does disclose the following data below (see col. 8 , ex. 10 , table 5 at con. of water=6 % ):

TABLE 5

Ex-ample	Pressure, psig	p-IBPE conversion, %	ibuprofen selectivity, %	n/iso	TOF, h <sup>-1</sup>
8	1000	99	96.70	0.0279	1190
9	500	98	94.00	0.0532	550
10	200	98	85.00	0.1600	200

By comparison, there is not much difference between the prior art and the current invention with the % conversion and the % selectivity of ibuprofen at low pressure. Therefore, the prior art reference is still relevant to the claimed invention.

Fourth, with respect to the sixth argument, the Examiner has noted applicants' argument. However, Elango et al does disclose a method of preparing ibuprofen by reacting 1-(4'-Isobutylphenyl)ethanol,  $\text{PdCl}_2(\text{PPh}_3)_2$ , HCl, lithium chloride as a halide source, and benzene in an autoclave at 125-129 °C. at a pressure of 500 psig. Similarly, Chaudhari et al discloses a process of preparing ibuprofen by reacting an aryl alcohol with tetrabutyl ammonium chloride as a halide source, protonic acid, water (4% v/v) palladium catalyst with a phosphine ligand in the presence of solvents such as N-methyl-pyrrolidone in a stirred reactor at a temperature of 70 to 175 °C and at a pressure of from 50 to 1500 psig.

Both are involved in the common process of preparing ibuprofen under similar reaction conditions (i.e. temperature and pressure, water, a halide source, palladium catalyst, etc.). Also, Chaudhari et al expressly indicates that there is an equivalency between tetrabutyl ammonium chloride and lithium chloride as for the halide source; in addition, it is possible to carry out the reaction in both biphasic medium and homogeneous medium (see col. 3, lines 19-24). Therefore, from these equivalencies, there is a motivation in the Chaudhari et al for combining the prior art. Therefore, it would have been obvious to the skillful artisan in the art to be motivated to use the Chaudhari's et al tetrabutyl ammonium chloride as an alternative for lithium chloride as well as the Chaudhari's et al water concentration in order to perform the reaction process in the homogeneous medium as a better alternative than the biphasic medium.



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This is because the skilled artisan in the art would expect the incorporation of the Chaudhari et al tetrabutyl ammonium chloride and water concentration into the Elango et al process to be a successful and improved process as shown in the Chaudhari et al.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

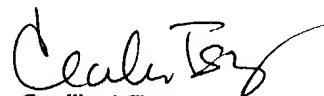
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax

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phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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12/07/04



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